

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

RECU

27-7-1999

PCT

To:

VAN MALDEREN, Eric
OFFICE VAN MALDEREN
Place Reine Fabiola 6/1
B-1083 Bruxelles
BELGIQUE

OFFICE VAN MALDEREN

NOTIFICATION OF RECEIPT OF DEMAND BY COMPETENT INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

(PCT Rules 59.3(e) and 61.1(b), first sentence
and Administrative Instructions, Section 601(a))

Date of mailing
(day/month/year)

27. 07. 1999

Applicant's or agent's file reference

P. FNDP. 03/WO

IMPORTANT NOTIFICATION

International application No.

PCT/ BE 98/ 00206

International filing date (day/month/year)

24/12/1998

Priority date (day/month/year)

30/12/1997

Applicant

REMACLE JOSE

1. The applicant is hereby **notified** that this International Preliminary Examining Authority considers the following date as the date of receipt of the demand for international preliminary examination of the international application:

16/07/1999

2. This date of receipt is:

- ☒ the actual date of receipt of the demand by this Authority (Rule 61.1(b)).
- ☐ the actual date of receipt of the demand on behalf of this Authority (Rule 59.3(e)).
- ☐ the date on which this Authority has, in response to the invitation to correct defects in the demand (Form PCT/IPEA/404), received the required corrections.

3. ☐ **ATTENTION:** That date of receipt is **AFTER** the expiration of 19 months from the priority date. Consequently, the election(s) made in the demand does (do) not have the effect of postponing the entry into the national phase until 30 months from the priority date (or later in some Offices) (Article 39(1)). Therefore, the acts for entry into the national phase must be performed within 20 months from the priority date (or later in some Offices) (Article 22). For details, see the *PCT Applicant's Guide*, Volume II.

- ☐ (If applicable) This notification confirms the information given by telephone, facsimile transmission or in person on:

4. Only where paragraph 3 applies, a copy of this notification has been sent to the International Bureau.

Name and mailing address of the IPEA/



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Netherlands
Tel.: (+31-70) 340-2040, Tx. 31 651 epo nl
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H. Daniels

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification⁶:

G01N 33/543, C12Q 1/68

A1

(11) International Publication Number:

WO 99/3549

(43) International Publication Date:

15 July 1999 (15.07.99)

(21) International Application Number: PCT/BE98/00206

(22) International Filing Date: 24 December 1998 (24.12.98)

(30) Priority Data:

60/071,726

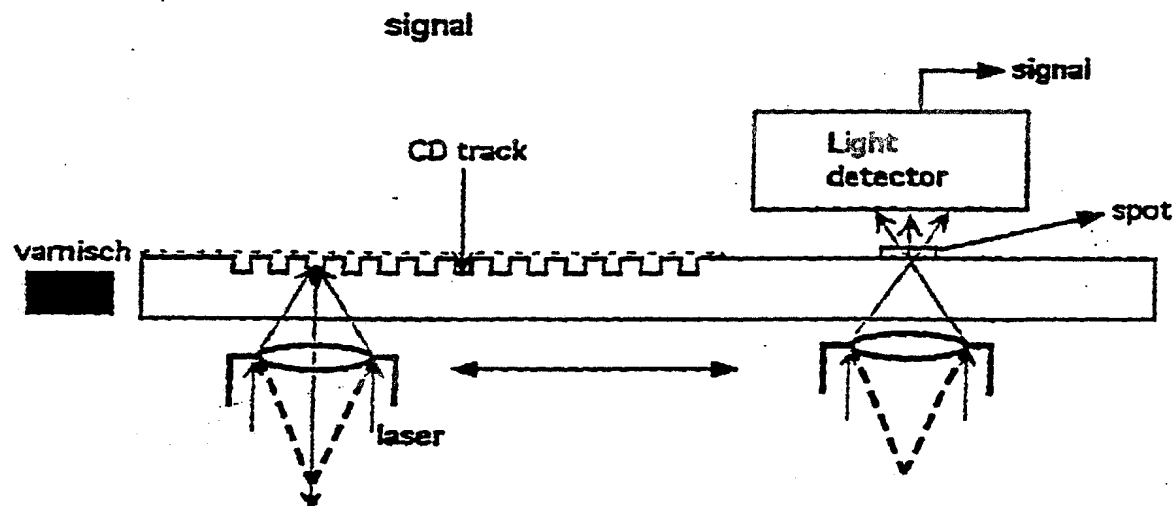
30 December 1997 (30.12.97) US

(71)(72) Applicant and Inventor: REMACLE, José [BE/BE];
Chemin des Pierres 14, B-5020 Malonne (BE).(74) Agents: VAN MALDEREN, Eric et al.; Office Van Malderen,
Place Reine Fabiola 6/1, B-1083 Brussels (BE).

(81) Designated States: AL, AM, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DE, DE (Utility model), EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published*With international search report.**Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.*

(54) Title: METHOD COMPRISING CAPTURE MOLECULE FIXED ON DISC SURFACE



(57) Abstract

The present invention is related to a method for the detection and/or the quantification of a target molecule by its binding with a non-cleavable capture molecule fixed on the surface of a disc comprising registered data. The present invention is also related to a disc having fixed upon its surface a non-cleavable capture molecule, to its preparation process, and to a diagnostic and/or reading device of said disc or comprising said disc.

PATENT COOPERATION TREATY

WO 99/35499
PCT/BE98/00206

PCT

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

From the INTERNATIONAL BUREAU

To:

VAN MALDEREN, Eric
Office Van Malderen
Place Reine Fabiola 6/1
B-1083 Brussels
BELGIQUE

Date of mailing (day/month/year) 15 July 1999 (15.07.99)		IMPORTANT NOTICE	
Applicant's or agent's file reference P.FNDP.03/WO			
International application No. PCT/BE98/00206	International filing date (day/month/year) 24 December 1998 (24.12.98)	Priority date (day/month/year) 30 December 1997 (30.12.97)	
Applicant REMACLE, José			

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
AU,CN,EP,IL,JP,KP,KR,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

**AL,AM,AP,BA,BB,BG,BR,CA,CU,CZ,DE,EA,EE,GD,GE,HR,HU,ID,IN,IS,LC,LK,LR,LT,LV,MG,MK,
MN,MX,NO,NZ,OA,PL,RO,SG,SI,SK,SL,TR,TT,UA,UZ,VN,XU**

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 15 July 1999 (15.07.99) under No. WO 99/35499

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a **demand for international preliminary examination** must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the **national phase**, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

<p style="text-align: center;">The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. (41-22) 740.14.35</p>	<p style="text-align: center;">Authorized officer J. Zahra</p> <p>Telephone No. (41-22) 338.83.38</p>
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Continuation of Form PCT/IB/308

**NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF
THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES**

Date of mailing (day/month/year) 15 July 1999 (15.07.99)	IMPORTANT NOTICE
Applicant's or agent's file reference P.FNDP.03/WO	International application No. PCT/BE98/00206

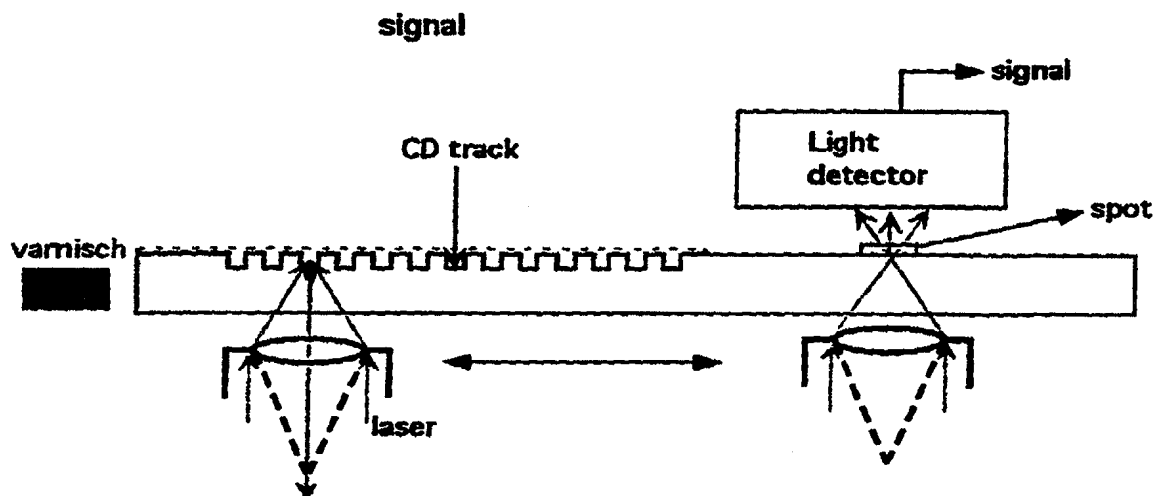
The applicant is hereby notified that, at the time of establishment of this Notice, the time limit under Rule 46.1 for making amendments under Article 19 has not yet expired and the International Bureau had received neither such amendments nor a declaration that the applicant does not wish to make amendments.



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶: G01N 33/543, C12Q 1/68	A1	(11) International Publication Number: WO 99/35499 (43) International Publication Date: 15 July 1999 (15.07.99)
(21) International Application Number: PCT/BE98/00206 (22) International Filing Date: 24 December 1998 (24.12.98) (30) Priority Data: 60/071,726 30 December 1997 (30.12.97) US (71)(72) Applicant and Inventor: REMACLE, José [BE/BE]; Chemin des Pierres 14, B-5020 Malonne (BE). (74) Agents: VAN MALDEREN, Eric et al.; Office Van Malderen, Place Reine Fabiola 6/1, B-1083 Brussels (BE).		(81) Designated States: AL, AM, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DE, DE (Utility model), EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>

(54) Title: METHOD COMPRISING CAPTURE MOLECULE FIXED ON DISC SURFACE

**(57) Abstract**

The present invention is related to a method for the detection and/or the quantification of a target molecule by its binding with a non-cleavable capture molecule fixed on the surface of a disc comprising registered data. The present invention is also related to a disc having fixed upon its surface a non-cleavable capture molecule, to its preparation process, and to a diagnostic and/or reading device of said disc or comprising said disc.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
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DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

INTERNATIONAL SEARCH REPORT

International Application No
PCT/BE 98/00206

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G01N33/543 C1201/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	EP 0 887 645 A (SUISSE ELECTRONIQUE MICROTECH ;PRIONICS AG (CH); SCHERRER INST PAU) 30 December 1998 see claims; figure 4E see column 8, line 12 - line 18 see page 11, line 51 - page 12, line 7 ---	1-29
P, X	EP 0 886 141 A (SUISSE ELECTRONIQUE MICROTECH ;PRIONICS AG (CH)) 23 December 1998 see claims; figure 4E see column 7, line 46 - line 56 see column 15, line 34 - line 41 --- -/--	1-29

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

&" document member of the same patent family

Date of the actual completion of the international search

20 May 1999

Date of mailing of the international search report

01/06/1999

Name and mailing address of the ISA

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Authorized officer

Routledge, B

INTERNATIONAL SEARCH REPORT

Int tional Application No
PC1/BE 98/00206

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No. --
P,X	<p>WO 98 15356 A (GORDON JOHN FRANCIS ;MOLECULAR DRIVES LIMITED (GB)) 16 April 1998 see claims see page 3, line 15 - line 16 see page 6, line 11 - line 24 see page 7, line 33 - page 8, line 15 see page 12, line 21 - page 13, line 19; figure 3 see page 18, line 16 - line 22</p>	1-29
P,X	<p>WO 98 12559 A (DEMERS JAMES P) 26 March 1998 see claims 2,5 see page 7, paragraph 2 see page 8, paragraph 3 - page 9, paragraph 1 see page 15, paragraph 2 - page 18, paragraph 2</p>	1-29
X	<p>WO 97 21090 A (GAMERA BIOSCIENCE) 12 June 1997 cited in the application see claims 1,14-21,30-63 see page 6, line 2 - line 7 see page 11, line 2 - line 28 see page 28, line 11 - page 29, line 14 see page 52, line 3 - page 53, line 30</p>	1-29
X	<p>WO 96 09548 A (GORDON JOHN FRANCIS ;UNIV DUNDEE (GB)) 28 March 1996 see claims see page 4, line 14 - page 5, line 8 see page 6, line 3 - line 17 see page 11, line 5 - line 20 see page 14, line 5 - line 18</p>	1-29

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/BE 98/00206

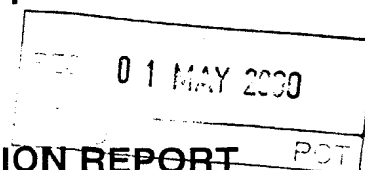
Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0887645 A	30-12-1998	EP 0886141 A	23-12-1998
EP 0886141 A	23-12-1998	EP 0887645 A	30-12-1998
WO 9815356 A	16-04-1998	AU 4564297 A	05-05-1998
WO 9812559 A	26-03-1998	AU 4428497 A	14-04-1998
WO 9721090 A	12-06-1997	AU 702403 B	18-02-1999
		AU 1283397 A	27-06-1997
		CA 2239613 A	12-06-1997
		EP 0865606 A	23-09-1998
		NO 982563 A	05-08-1998
		AU 4144897 A	06-03-1998
		WO 9807019 A	19-02-1998
WO 9609548 A	28-03-1996	AU 3481595 A	09-04-1996
		BR 9509021 A	30-12-1997
		CA 2200562 A	28-03-1996
		CN 1158659 A	03-09-1997
		EP 0782705 A	09-07-1997
		JP 10504397 T	28-04-1998
		US 5892577 A	06-04-1999

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference P.FNDP.03/WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/BE98/00206	International filing date (day/month/year) 24/12/1998	Priority date (day/month/year) 30/12/1997
International Patent Classification (IPC) or national classification and IPC G01N33/543		
Applicant REMACLE JOSE		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 14 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 16/07/1999	Date of completion of this report <div style="text-align: center; font-size: 1.5em;">21 04 00</div>
Name and mailing address of the international preliminary examining authority: <div style="display: flex; align-items: center;"> <div> European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016 </div> </div>	Authorized officer Routledge, B Telephone No. +31 70 340 4272



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/BE98/00206

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-3,4.1 (part),5, as originally filed
6,8,9,11,13-26,
31

4bis,4ter,7	as received on	04/02/2000	with letter of	01/02/2000
10,12,27-30	with telefax of	27/03/2000		

Claims, No.:

1-29	as received on	04/02/2000	with letter of	01/02/2000
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Drawings, sheets:

1/3-3/3 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/BE98/00206

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-29	YES
	No:	Claims		
Inventive step (IS)	Yes:	Claims	1-29	YES
	No:	Claims		
Industrial applicability (IA)	Yes:	Claims		
	No:	Claims	1-29	YES

2. Citations and explanations

see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/BE98/00206

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The application meets the criteria of Article 33(2) and (3) PCT in that claims 1-29 are novelty and inventive. The use and production of a solid support disc comprising an area on a surface of a solid support containing a non cleavable capture molecule for binding a target molecule and a separate area on the solid support disc for registered data, wherein the results from the binding and registered data areas are read using different reading devices is neither disclosed nor suggested in the cited prior art.
2. **WO 97/21090** discloses an optical sensor unit in disk form having a noncleavable capture molecule thereon and information. Binding is detected by a single optical system. Moreover, the binding reaction takes place in microchannels embedded in the surface of the disc and not on the surface itself which leads to difficulties in reading the result of the binding reaction due to diffusion of the light beam through the surface material before reaching the microchannels. **WO 96/09548** discloses use of the compact disc format to detect ELISA reactions. Address and location information is obtained from the modulation of the binding signal.
3. All claims meet the criteria of Article 33(4) PCT with regard to industrial applicability.

Re Item VI

Certain documents cited

Certain published documents (Rule 70.10)

1. Patent No: EP 0 887 645 Publication date: 30.12.98
Filing date: 23.06.97

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/BE98/00206

2. Patent No: EP 0 886 141 Publication date: 23.12.98
Filing date: 03.06.98
Priority date (valid claim): 23.06.97
3. Patent No: WO 98/15356 Publication date: 16.04.98
Filing date: 08.10.97
Priority date (valid claim): 08.10.96
4. Patent No: WO 98/12559 Publication date: 23.03.98
Filing date: 19.09.97
Priority date (valid claim): 20.09.96

EP 0 887 645 and **EP 0 886 141** both disclose optical sensor units (disc, CD having reference information thereon) with a biochemical ligand attached and binding being detected.

WO 98/15356 discloses a disc attachable to a CD having location information, said disc having microchannels and whereon binding reaction takes places which is optically detected.

WO 98/12559 discloses the synthesis of molecules on a CD having location address information. The binding of the synthesised molecules with an analyte of interest is optically detected.

None of the above documents discloses a solid support disc comprising an area on a surface of a solid support containing a non cleavable capture molecule for binding a target molecule and a separate area on the solid support disc for registered data, wherein the results from the binding and registered data areas are read using different reading devices.

Re Item VIII

Certain observations on the international application

1. The application does not meet the requirements of Article 6 PCT in that the scope of the claims lacks clarity. The precise meaning of the phrase "...registered data"

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/BE98/00206

used extensively throughout the claims and description is vague and obscure. It would appear to include any data relating to any aspect of control of the disc, address location of the capture molecules or details of experimental protocols and results (see pages **5, 7, 8, 18** and **19**). The ambiguity is compounded by the use of "possibly" in claim **25** with regard to the presence of reactants and on pages **5** and **7** which could be interpreted to mean that the presence of the data on the disc is not an essential characterising feature.

1.1 In addition, the application does not meet the requirements of Article 6 PCT for the following reasons:-

- (a) The features "radiation" claim **7**, "radioactivity" claim **8**, "magnetic particle" claim **11**, "fluidic contact" claims **16** and **21** and the subject matter of claims **26-28** are not clearly supported in the body of the description.
- (b) The dependency of claim **21** is incorrect.
- (c) The embodiments concerned with the use of microchannels disclosed on pages **14** and **20** are inconsistent with the acknowledged fact distinguishing the present application from the cited prior art that the presence of microchannels renders reading of the result of binding of the target molecule difficult.

REPLACED BY
ART 34 AMDT

adapted to bind a first site on a chosen analyte and a second side member adapted to bind a second site of said chosen analyte. The signal is measured when the analyte is fixed upon the first side member and the second side member. Thereafter, the spacer is cleaved and the fixation of the analyte allows the detection of a positive signal.

However, this complex and expensive detection method and device is submitted to various false positives or false negatives in the detection of various complex analytes, which could develop various interactions with said cleavable signal elements.

Summary of the invention

The present invention is related to a method for the detection and/or the quantification of a target molecule as described in the claims.

The present invention is also related to a disc having fixed upon its surface a non-cleavable capture molecule as described in the claims, and which can be used in the detection and/or quantification method according to the invention.

Another aspect of the present invention is related to a preparation process of said disc, a diagnostic kit comprising said disc, a diagnostic and reading device comprising said disc or a diagnostic and reading device which allows the reading and the analysis of the data present upon the disc according to the invention.

Technical characteristics of the "disc"

By the term "disc" is meant a flat solid support (usually in the form of a disc) which comprises a hole that allows its rotation according to an axis (A)

communications with remote display or data analysis systems.

One remarkable aspect of the disc according to the invention is the density of the microscopic array of possibly pre-registered data patterns embedded within the disc materials. It is an optical storage using a laser beam to detect impressions in the surface of the reflective disc. The ability to compress data to such a fine degree and read it back accurately gives the disc according to the invention one of its defining characteristics, the capability of storing huge amounts of data (for a compact-disc of audio data, the amount of storing is around 650 MB of data).

The disc according to the invention could be adapted for the penetration and refraction of various laser beams upon various polymeric or metallic layers.

For example, laser devices used for emission of a laser beam and detection of a reflected laser beam may advantageously comprise a hologram disposed between the disc and a photometre.

The disc is in general of 1.2 mm thick and 4.72 inches in diameter, but smaller supports also exist and could be adapted for specific applications (such as binding between a capture and a target molecules into a Petri dish), and the thickness can be adapted according to the technical requirements of the capture molecule and the detection method of the invention used.

The disc can incorporate grooves to conduct the lecture by a laser beam. In said grooves are incorporated "registered" data that can be thereafter analyzed and advantageously transcribed into digital data. Preferably, said registered data are in the form of binary

said layer without difficulty and to detect the binding between a "target" molecule and its "capture" molecule or the result of said binding. If necessary, said layer may be omitted before or after the binding between capture and
5 target molecules.

To successfully communicate by means of nothing than a series of pits in a disc requires computer processing and some already available high-technology wizardry. At no point does the laser's read mechanism ever
10 touch the disc surface; all data is preferably conveyed by reflections of the laser. In a normal audio CD, the laser beam takes a certain amount of time to return when it is reflected off the lands, but it takes longer to travel if it is swallowed up and reflected by pits. The depth of the
15 pit is engineered to be $1/4$ the wavelength of the laser light. If the reflected beam from the pit cancels out the beam from the land, a signal transition is obtained. Signal transitions (signaled by the beginning or end of a pit) represent binary 1's. If there is no signal transition,
20 this indicates a binary 0.

One particular feature of commercial CD-drives is their property to read such pits and deliver data at unpriseve 900 Kb/sec, making this laser reflector technology particularly suitable for the reading not only
25 of the registered pits but also the result of the binding.

To maintain synchronization while reading the data patterns, the CD drive uses self-clocking mechanism that is commonly found in hard disk drives, which is called
Run Length Limited. Because data exists within finite
30 divisions on the spiral track, each data division extends approximately 300 nanometers, the CD-microcontroller can produce regular clock signals by synchronizing to the speed

Specific areas of the disc according to the invention can be dedicated to the reading of the reaction that is the result of the binding between the target and the capture molecules. These specific areas are parts of the disc surface according to the invention or an area of the disc on which a second material is fixed and whose surface comprises the capture molecules. These areas can be a cavity in the disc. Said second material is a strip of plastic upon which the binding between the target and the capture molecules has already been performed and which is thereafter fixed upon the disc for its specific reading.

Advantageously, each strip can be loaded with several different capture molecules that will react specifically with the same sample or different samples to be analyzed. Thereafter, the signal can be read individually or simultaneously upon the same disc. A classical disc like a compact-disc could be able to handle 20 or more of such strips.

Preferred embodiments that are most advantageous for manufacturing and operation of the compact-disc of the invention have dimensions within one or more of four pre-existing formats :

- 3-inch compact disk (CD), having a radius of about 3.8 cm and thickness of about 1 mm,
- 5-inch CD, having a radius of about 6 cm and a thickness of 1 mm,
- 8-inch CDV (commercially termed a "Laservision" disk), having a radius of 10 cm and a thickness of 2 mm, and
- 12-inch CDV disk, having a radius of 15 cm and a thickness of 2 mm.

2. Fixation of capture probes on aminated CDs

2 solutions were prepared, one containing CMV capture probe and the other containing HIV capture probe. These solutions were MeIM 0.01 M pH 7.5 buffer containing
5 denatured DNA capture probe (CMV or HIV) at a concentration of 2 $\mu\text{g/ml}$ and carbodiimide at a concentration of 1.6 mg/ml.

3 x 20 μl of these solutions were spotted on two aminated CDs and these CDs were incubated at 50 $^{\circ}\text{C}$ for
10 5 hours in a wet atmosphere. After three washes of 5 min with NaOH 0.4 N + Tween 0.25% at 50 $^{\circ}\text{C}$, these CDs were rinsed 3 times with water and dried at 37 $^{\circ}\text{C}$ for 30 min.

3. Hybridization of CMV biotinylated DNA on CDs

Both CDs were incubated 5 min in NaOH 0.2 N for denaturing capture probe, then rinsed with 0.1 M maleate buffer pH 7.5 with 0.15 M NaCl. These CDs were then incubated in a hybridization solution containing
15 denatured DNA salmon sperm 100 $\mu\text{g/ml}$, SSC 4X, Denhardt 5X and denatured CMV biotinylated DNA at a concentration of
20 70 ng/ml for 2 hours at 65 $^{\circ}\text{C}$. After hybridization step, the CDs were washed 3 times with 0.01 M maleate buffer containing 15 mM NaCl and Tween 0.3% at room temperature.

The first CD was then incubated with 0.1 M maleate buffer containing 0.15 M NaCl, 0.1% milk powder and
25 streptavidin-peroxidase 1 $\mu\text{g/ml}$ for 45 min at room temperature. After conjugates incubation, both CDs were washed 3 times with 0.01 M maleate buffer containing 15 mM NaCl and Tween 0.3% at room temperature.

4. Detection of hybridized DNA

The first CD was then incubated for 10 min in TMB solution (Medgenix). A picture was taken of this CD after 1 min of this incubation to see blue color appearing where positive hybridization occurred (Fig. 4). The result can be obtained by absorption of transmitted light through the CD.

Example 2: Detection of DNA on CD with maser detection

The DNA capture probe was spotted on the CD surface and the hybridization with the target DNA were identical to the example 1. For the detection of the biotinylated hybridized DNA, the CD was incubated with 0.1 M maleate buffer containing 0.15 M NaCl, 0.1% milk powder and streptavidin-colloidal gold (Sigma, St-Louis, USA) 1 μ g/ml for 45 min at room temperature. The CD was further incubated 30 min in a solution made of equal volume of Solution A and B from Silver enhancement kit (Sigma, St-Louis, USA) in order to have silver precipitate where positive hybridization occurred. This CD was recovered with a gold layer to allow a laser CD player to read information written on the CD and to read the interference due to silver precipitate (Fig. 2 and 3).

Example 3: Detection of protein on CD by light absorption

The CD used were partly inprinted with data on pits and this part was covered with gold. The fixation of the capture molecules was done on the periphery of the CD, directly on the plastic surface.

1. Carboxylation of CD

First CDs were incubated 30 min in NaOH 1 N at room temperature then rinsed 3 times with water and dried at 37 °C for 30 min.

5

2. Fixation of antibodies on CDs

Three different types of antibodies were fixed on the carboxylated CD: antibodies against bovine serum albumin, antibodies against fluoresceine (for
10 negative control) and antibodies against streptavidin (for positive control).

20 µl of three different solutions of borate buffer 0.02 M NaCl pH 8.2 containing carbodiimide (Acros) at 1 mg/ml and one type of the three different antibodies
15 at 10 µg/ml were spotted on three different pieces of CD. These spots were incubated overnight at 4 °C, and then rinsed for 10 min with glycine buffer 0.1 M pH 9.2 containing casein at 0.1%, then twice with glycine buffer 0.1 M pH 9.2 containing Tween 20 at 0.1% for 5 min and
20 finally twice with glycine buffer 0.1 M pH 9.2. The CDs were dried at 37 °C during 30 min.

3. Detection of bovine serum albumin by ELISA technique on CD

25 The CDs were incubated at room temperature with the three different antibodies fixed onto the surface with a solution of serum albumin at 10 µg/ml in PBS containing 0.1% of casein. The incubation was for 90 min. The CDs were rinsed 3 times with PBS containing 0.1% of
30 Tween 20, and then incubated with biotinylated antibodies against serum albumin at 20 µg/ml in PBS containing 0.1% of

casein for 45 min. They were then rinsed 3 times with PBS containing 0.1% of Tween 20, and then incubated for 45 min the CDs in a solution of PBS containing 0.1% of casein and either Streptavidin-peroxidase at 1 $\mu\text{g/ml}$. The CDs were
5 rinsed 3 times with PBS containing 0.1% of Tween 20. For detection, the CD where streptavidin-peroxidase was fixed were incubated in a solution of TMB and pictures were taken after 2, 4 and 6 min under camera to see blue color appearing where we had spotted antibodies against BSA and
10 against streptavidin.

Example 4: Detection of proteins on CD with laser detection

The albumin was spotted on the CD surface and the reaction with the antibodies were identical to the
15 example 3. The conjugate used to react against the biotinylated antibodies was a streptavidin-gold. It. was incubated for 45 min in a PBS solution containing 0.1% casein at a concentration of 1 $\mu\text{g/ml}$. The streptavidin-gold served as a center for silver reduction. A solution of
20 "silver enhancement" (Sigma) for 15 min at room temperature was used. Silver precipitation was seen at the place where antibodies against BSA and against streptavidin were spotted. A variation in the light absorption was observed, due to the precipitate and the size of the precipitate
25 which are about 1 μm in diameter. The presence of pits was found by reflection of the laser beam (Fig. 5).

Example 5: Magnetic detection of DNA or protein on CD

Detection of hybridized DNA or protein on CD
30 support can be achieved by magnetic process. Biotin bound to DNA or antibodies can be recognized by streptavidin conjugated to ferro-fluid (Immunicon, Hungtinton Valley,

CLAIMS

1. Method for the detection and/or the quantification of a target molecule present in a sample, preferably a biological sample, comprising the steps of :

- 5 - allowing a binding between said target molecule and a capture molecule fixed upon the surface of a solid support being a disc comprising registered data, said binding resulting in a signal,
- allowing a detection and/or quantification of said signal
- 10 with the proviso that said signal is not obtained through cleavage of capture molecule.

2. Method according to claim 1, characterized in that the capture and the target molecules are nucleotide sequences.

- 15 3. Method according to claim 1, characterized in that the capture and target molecules are respectively either antigens or antibodies.

4. Method according to claim 1, characterized in that the capture and target molecules are respectively

20 either receptors or ligands of said receptors.

5. Method according to any one of the preceding claims, characterized in that the detection and/or the quantification of the signal is obtained by reflection, absorption or diffraction of a light beam,

25 preferably a laser beam, or variation of an electromagnetic field.

6. Method according to any one of the preceding claims, characterized in that the detection and/or the quantification of the signal is obtained by a

30 fluorescent light emission after excitation of the bound target and capture molecules by a light beam.

7. Method according to any one of the claims 1 to 4, characterized in that the detection and/or the quantification of the signal is obtained by a direct emission of a light beam, a radiation or a magnetic field, which is a result of the binding between the target molecule and its capture molecule.

8. Method according to claim 6 or 7, characterized in that the emission of a light beam is generated by a bound molecule which is selected from the group consisting of molecules having chemo, bio, fluoro, radioactivity and/or electroluminescence light or radiation.

9. Method according to any one of the preceding claims, characterized in that the binding between the target and the capture molecules generates a precipitate, preferably an opaque or magnetic precipitate such as a deposit of a colloidal metal reagent, preferably a silver precipitate, upon the surface of the disc and/or the corrosion of one or more layer(s) of the surface of the disc.

10. Method according to any one of the preceding claims, characterized in that the binding between the target and the non-cleavable capture molecules allows the fixation of one or more molecule(s) used in the detection and/or the quantification of a signal which results from said binding.

11. Method according to claim 10, characterized in that said other molecule is a microbead or a magnetic particle.

12. Method according to any one of the preceding claims, characterized in that the signal is obtained when the disc is rotating upon its axis (A).

13. Method according to any one of the preceding claims, characterized in that the registered data of the disc are binary data, preferably grooved binary data.

5 14. Method according to any one of the preceding claims, characterized in that the disc is a compact-disc.

15 15. Method according to any one of the preceding claims, characterized in that the registered data
10 allow the treatment and the interpretation of the signal resulting from the binding between the capture and the target molecules.

16. Method according to any one of the preceding claims, characterized in that the disc comprises
15 micro-channels connected and in fluidic contact.

17. Disc comprising registered data, characterized in that it further comprises, fixed upon its surface, a non-cleavable capture molecule which allows a binding with a target molecule to be detected and/or
20 quantified.

18. Disc according to claim 17, characterized in that the non-cleavable capture and/or the target molecules are selected from the group consisting of nucleic acid molecules, preferably nucleotide sequences, antigens,
25 antibodies, receptors, ligands of receptors, peptidic or proteinic molecules, lipids, saccharides, haptens, fluorophores, chromophores, catalysts, new macromolecules obtained by combinatorial chemistry or a combination thereof.

30 19. Disc according to claim 17 or 18, characterized in that the registered data of the disc are binary data, preferably grooved binary data.

20. Disc according to claim 19, characterized in that it is a compact-disc.

21. Disc according to any one of the claims any of the claims 17 to 21, characterized in that it
5 comprises microchannels connected and in fluidic contact.

22. Preparation process of the disc according to any one of the claims 17 to 21, which comprises the step of a fixation upon the surface of a disc comprising pre-registered data of a non-cleavable capture molecule through
10 a photoactivation of said capture molecule.

23. Process according to claim 22, characterized in that the non-cleavable capture molecule is obtained through a covalent link between an extremity of the capture molecule and the surface layer of the disc.

15 24. Process according to claim 22 or 23, characterized in that the disc surface is recovered by a protective layer, preferably made of organic compound, which allows or improves the protection and stabilization of the non-cleavable capture molecule and/or the
20 protection, stabilization and/or detection of the binding between the target molecule and its non-cleavable capture molecule.

25 25. Diagnostic kit comprising the disc according to any one of the claims 17 to 21 and the reactants allowing the binding between a target molecule and its capture molecule and possibly the reactants allowing the detection of the signal which results from said binding.

30 26. Detection and/or reading device which allows the detection and/or the quantification of the signal which results from the binding between a target molecule present in a sample and its capture molecule, and

which comprises the disc according to any one of the claims 17 to 21 or the kit according to claim 25, and means for the detection and/or quantification of said signal.

27. Detection and/or reading device according
5 to claim 26, being a reading compact-disc device.

28. Detection and/or reading device according
to claim 27, characterized in that it comprises a first
reading head for the reading of registered data upon the
disc and a second reading head for the detection and/or the
10 quantification of the signal which results from the binding
between target molecule and its capture molecule.

29. Detection and/or reading device according
to any one of the claims 26 to 28, which comprises
additional means for the purification of the target
15 molecule, the specific cleavage of the target molecule, the
possible genetic amplification of said target molecule
within an integrated detection and/or reading device.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P.FNDP.03/WO		FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/BE98/00206	International filing date (day/month/year) 24/12/1998	Priority date (day/month/year) 30/12/1997	
International Patent Classification (IPC) or national classification and IPC G01N33/543			
Applicant REMACLE JOSE			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 6 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 14 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 16/07/1999	Date of completion of this report 21. 04. 00
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer Routledge, B Telephone No. +31 70 340 4272 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/BE98/00206

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-3,4.1 (part),5, as originally filed
6,8,9,11,13-26,
31

4bis,4ter,7	as received on	04/02/2000	with letter of	01/02/2000
10,12,27-30	with telefax of	27/03/2000		

Claims, No.:

1-29	as received on	04/02/2000	with letter of	01/02/2000
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Drawings, sheets:

1/3-3/3 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/BE98/00206

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 1-29	YES
	No:	Claims	
Inventive step (IS)	Yes:	Claims 1-29	YES
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	
	No:	Claims 1-29	YES

-?

2. Citations and explanations

see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/BE98/00206

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The application meets the criteria of Article 33(2) and (3) PCT in that claims 1-29 are novelty and inventive. The use and production of a solid support disc comprising an area on a surface of a solid support containing a non cleavable capture molecule for binding a target molecule and a separate area on the solid support disc for registered data, wherein the results from the binding and registered data areas are read using different reading devices is neither disclosed nor suggested in the cited prior art.
2. **WO 97/21090** discloses an optical sensor unit in disk form having a noncleavable capture molecule thereon and information. Binding is detected by a single optical system. Moreover, the binding reaction takes place in microchannels embedded in the surface of the disc and not on the surface itself which leads to difficulties in reading the result of the binding reaction due to diffusion of the light beam through the surface material before reaching the microchannels. **WO 96/09548** discloses use of the compact disc format to detect ELISA reactions. Address and location information is obtained from the modulation of the binding signal.
3. All claims meet the criteria of Article 33(4) PCT with regard to industrial applicability.

Re Item VI

Certain documents cited

Certain published documents (Rule 70.10)

1. Patent No: EP 0 887 645 Publication date: 30.12.98
Filing date: 23.06.97

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/BE98/00206

2. Patent No: EP 0 886 141 Publication date: 23.12.98
Filing date: 03.06.98
Priority date (valid claim): 23.06.97
3. Patent No: WO 98/15356 Publication date: 16.04.98
Filing date: 08.10.97
Priority date (valid claim): 08.10.96
4. Patent No: WO 98/12559 Publication date: 23.03.98
Filing date: 19.09.97
Priority date (valid claim): 20.09.96

EP 0 887 645 and **EP 0 886 141** both disclose optical sensor units (disc, CD having reference information thereon) with a biochemical ligand attached and binding being detected.

WO 98/15356 discloses a disc attachable to a CD having location information, said disc having microchannels and whereon binding reaction takes places which is optically detected.

WO 98/12559 discloses the synthesis of molecules on a CD having location address information. The binding of the synthesised molecules with an analyte of interest is optically detected.

None of the above documents discloses a solid support disc comprising an area on a surface of a solid support containing a non cleavable capture molecule for binding a target molecule and a separate area on the solid support disc for registered data, wherein the results from the binding and registered data areas are read using different reading devices.

Re Item VIII

Certain observations on the international application

1. The application does not meet the requirements of Article 6 PCT in that the scope of the claims lacks clarity. The precise meaning of the phrase "...registered data"

used extensively throughout the claims and description is vague and obscure. It would appear to include any data relating to any aspect of control of the disc, address location of the capture molecules or details of experimental protocols and results (see pages 5, 7, 8, 18 and 19). The ambiguity is compounded by the use of "possibly" in claim 25 with regard to the presence of reactants and on pages 5 and 7 which could be interpreted to mean that the presence of the data on the disc is not an essential characterising feature.

1.1 In addition, the application does not meet the requirements of Article 6 PCT for the following reasons:-

- (a) The features "radiation" claim 7, "radioactivity" claim 8, "magnetic particle" claim 11, "fluidic contact" claims 16 and 21 and the subject matter of claims 26-28 are not clearly supported in the body of the description.
- (b) The dependency of claim 21 is incorrect.
- (c) The embodiments concerned with the use of microchannels disclosed on pages 14 and 20 are inconsistent with the acknowledged fact distinguishing the present application from the cited prior art that the presence of microchannels renders reading of the result of binding of the target molecule difficult.

adapted to bind a first site on a chosen analyte and a second side member adapted to bind a second site of said chosen analyte. The signal is measured when the analyte is fixed upon the first side member and the second side member. Thereafter, the spacer is cleaved and the fixation of the analyte allows the detection of a positive signal.

However, this complex and expensive detection method and device is submitted to various false positives or false negatives in the detection of various complex analytes, which could develop various interactions with said cleavable signal elements.

The document WO97/21090 describes a disc comprising a solid support, an entrance for a biological sample to be analyzed and inside said solid support microchannels for the various treatments of said sample. The other side of said flat solid support in the form of a disc comprises electromagnetic encoded instructions for the control of the rotation of said disc. The biological sample is present in a fluid which can be dedicated to various microchannels according to a centripetal movement.

The document WO96/09548 an apparatus and method for carrying out analysis of biological, chemical or biochemical samples upon an optical transparent disc. Said general optical analysis technique could be adapted to a compact disc by scanning its surface to which a sample has been attached, with a light beam which is substantially focused on that surface. Position codes can be imprinted at discrete regions around the innermost track, incrementing by one between each position. The codes are incremented from track to track. Alternatively, address information may be distributed according to a track sector arrangement in the same way and servo-codes are encoded onto magnetic floppy and hard disks. In said system, any biological material attached to the upper surface will be interfered

with light exciting the disc. Light reflected by the reflective layer will be modulated with the information digitally encoded into the disc so that the output of the detector will be similarly modulated.

5

Summary of the invention

The present invention is related to a method for the detection and/or the quantification of a target molecule as described in the claims.

10

The present invention is also related to a disc having fixed upon its surface a non-cleavable capture molecule as described in the claims, and which can be used in the detection and/or quantification method according to the invention.

15

Another aspect of the present invention is related to a preparation process of said disc, a diagnostic kit comprising said disc, a diagnostic and reading device comprising said disc or a diagnostic and reading device which allows the reading and the analysis of the data

20

present upon the disc according to the invention.

Technical characteristics of the "disc"

By the term "disc" is meant a flat solid support (usually in the form of a disc) which comprises a hole that allows its rotation according to an axis (A)

25

communications with remote display or data analysis systems.

One remarkable aspect of the disc according to the invention is the density of the microscopic array of possibly pre-registered data patterns embedded within the disc materials. It is an optical storage using a laser beam to detect impressions in the surface of the reflective disc. The ability to compress data to such a fine degree and read it back accurately gives the disc according to the invention one of its defining characteristics, the capability of storing huge amounts of data (for a compact-disc of audio data, the amount of storing is around 650 MB of data).

The disc according to the invention could be adapted for the penetration and refraction of various laser beams upon various polymeric or metallic layers.

For example, laser devices used for emission of a laser beam and lecture of a reflected laser beam may advantageously comprise a hologram disposed between the disc and a photometre.

The disc is in general of 1.2 mm thick and ~~4.72 inches~~ ^{1.9 cm} in diameter, but smaller supports also exist and could be adapted for specific applications (such as binding between a capture and a target molecules into a Petri dish), and the thickness can be adapted according to the technical requirements of the capture molecule and the detection method of the invention used.

The disc can incorporate grooves to conduct the lecture by a laser beam. In said grooves are incorporated "registered" data that can be thereafter analyzed and advantageously transcribed into digital data. Preferably, said registered data are in the form of binary

AMENDED SHEET
IPEA/EP

5

CLAIMS

1. Method for the detection and/or the quantification of a target molecule present in a sample, preferably a biological sample, comprising the steps of :

- allowing a binding between said target molecule and a capture molecule fixed upon a side of the surface of a solid support being a disc comprising registered data, said binding resulting in a signal, the registered data being located on areas separated from the areas dedicated to the reading of the signal resulting from the binding of a target molecule and a capture molecule,
- allowing a detection and/or quantification of said signal with the proviso that said signal is not obtained through cleavage of capture molecule, and
- reading the registered information and reading the signal resulting from the binding between a target molecule and a capture molecule said readings being done by two different reading devices.

2. Method according to claim 1, characterized in that the capture and the target molecules are nucleotide sequences.

3. Method according to claim 1, characterized in that the capture and target molecules are respectively either antigens or antibodies.

4. Method according to claim 1, characterized in that the capture and target molecules are respectively either receptors or ligands of said receptors.

5. Method according to any one of the preceding claims, characterized in that the detection and/or the quantification of the signal is obtained by reflection, absorption or diffraction of a light beam,

preferably a laser beam, or variation of an electromagnetic field.

6. Method according to any one of the preceding claims, characterized in that the detection
5 and/or the quantification of the signal is obtained by a fluorescent light emission after excitation of the bound target and capture molecules by a light beam.

7. Method according to any one of the claims
1 to 4, characterized in that the detection and/or the
10 quantification of the signal is obtained by a direct emission of a light beam, a radiation or a magnetic field, which is a result of the binding between the target molecule and its capture molecule.

8. Method according to claim 6 or 7,
15 characterized in that the emission of a light beam is generated by a bound molecule which is selected from the group consisting of molecules having chemo, bio, fluoro, radioactivity and/or electroluminescence light or radiation.

9. Method according to any one of the preceding claims, characterized in that the binding between the target and the capture molecules generates a precipitate, preferably an opaque or magnetic precipitate such as a deposit of a colloidal metal reagent, preferably
25 a silver precipitate, upon the surface of the disc and/or the corrosion of one or more layer(s) of the surface of the disc.

10. Method according to any one of the preceding claims, characterized in that the binding between
30 the target and the non-cleavable capture molecules allows the fixation of one or more molecule(s) used in the detection and/or the quantification of a signal which results from said binding.

11. Method according to claim 10,
35 characterized in that the binding between the target and

the non-cleavable capture molecule allows the fixation of one or more microbeads or magnetic particles used in the detection and/or the quantification of a signal that results from said binding.

5 12. Method according to any one of the preceding claims, characterized in that the signal is obtained when the disc is rotating upon its axis (A).

10 13. Method according to any one of the preceding claims, characterized in that the registered data of the disc are binary data, preferably grooved binary data.

 14. Method according to any one of the preceding claims, characterized in that the disc is a compact-disc.

15 15. Method according to any one of the preceding claims, characterized in that the registered data are data used in the treatment and the interpretation of the signal resulting from the binding between the capture and the target molecules.

20 16. Method according to any one of the preceding claims, characterized in that the disc comprises micro-channels connected and in fluidic contact.

 17. Disc comprising registered data, characterized in that it further comprises, fixed upon a side of its surface, in dedicated areas different from the areas comprising registered data, non-cleavable capture molecules that allow a binding with target molecules to be detected and/or quantified.

25 18. Disc according to claim 17, characterized in that the non-cleavable capture and/or the target molecules are selected from the group consisting of nucleic acid molecules, preferably nucleotide sequences, antigens, antibodies, receptors, ligands of receptors, peptidic or proteinic molecules, lipids, saccharides, haptens, 35 fluorophores, chromophores, catalysts, new macromolecules

obtained by combinatorial chemistry or a combination thereof.

19. Disc according to claim 17 or 18, characterized in that the registered data of the disc are
5 binary data, preferably grooved binary data.

20. Disc according to claim 19, characterized in that it is a compact-disc.

21. Disc according to any one of the claims any of the claims 17 to 21, characterized in that it
10 comprises microchannels connected and in fluidic contact.

22. Preparation process of the disc according to any one of the claims 17 to 21, which comprises the step of a fixation upon a side of the surface of a disc comprising registered data, of non-cleavable capture
15 molecules at specific dedicated areas different from the areas comprising registered data, through a photoactivation of said capture molecules.

23. Process according to claim 22, characterized in that the fixation of non-cleavable capture
20 molecules is obtained through a covalent link between an extremity of the capture molecules and the surface layer of the disc.

24. Process according to claim 22 or 23, characterized in that the disc surface comprises a
25 protective layer, preferably made of organic compound, which allows or improves the protection and stabilization of the non-cleavable capture molecule and/or the protection, stabilization and/or detection of the binding between the target molecule and its non-cleavable capture
30 molecule.

25. Diagnostic kit comprising the disc according to any one of the claims 17 to 21 and the reactants allowing the binding between a target molecule and its capture molecule and possibly the reactants

allowing the detection of the signal which results from said binding.

5 26. Detection and/or reading device which allows the detection and/or the quantification of the signal which results from the binding between a target molecule present in a sample and its capture molecule, and which comprises the disc according to any one of the claims 17 to 21 or the kit according to claim 25, and means for the detection and/or quantification of said signal.

10 27. Detection and/or reading device according to claim 26, being a reading compact-disc device.

15 28. Detection and/or reading device according to claim 27, characterized in that it comprises a first reading head for the reading of registered data upon the disc and a second reading head for the detection and/or the quantification of the signal which results from the binding between target molecule and its capture molecule.

20 29. Detection and/or reading device according to any one of the claims 26 to 28, which comprises additional means for the purification of the target molecule, the specific cleavage of the target molecule, the possible genetic amplification of said target molecule within an integrated detection and/or reading device.

said layer without difficulty and to detect the binding between a "target" molecule and its "capture" molecule or the result of said binding. If necessary, said layer may be omitted before or after the binding between capture and
5 target molecules.

To successfully communicate by means of nothing than a series of pits in a disc requires computer processing and some already available high-technology wizardry. At no point does the laser's read mechanism ever
10 touch the disc surface; all data is preferably conveyed by reflections of the laser. In a normal audio CD, the laser beam takes a certain amount of time to return when it is reflected off the lands, but it takes longer to travel if it is swallowed up and reflected by pits. The depth of the
15 pit is engineered to be $1/4$ the wavelength of the laser light. If the reflected beam from the pit cancels out the beam from the land, a signal transition is obtained. Signal transitions (signaled by the beginning or end of a pit) represent binary 1's. If there is no signal transition,
20 this indicates a binary 0.

One particular feature of commercial CD-drives is their property to read such pits and deliver data at 900 Kb/sec, making this laser reflector technology particularly suitable for the reading not only of the
25 registered pits but also the result of the binding.

To maintain synchronization while reading the data patterns, the CD drive uses self-clocking mechanism that is commonly found in hard disk drives, which is called Run Length Limited. Because data exists within finite
30 divisions on the spiral track, each data division extends approximately 300 nanometers, the CD-microcontroller can produce regular clock signals by synchronizing to the speed

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Specific areas of the disc according to the invention can be dedicated to the reading of the reaction that is the result of the binding between the target and the capture molecules. These specific areas are parts of the disc surface according to the invention or an area of the disc on which a second material is fixed and whose surface comprises the capture molecules. These areas can be a cavity in the disc. Said second material is a strip of plastic upon which the binding between the target and the capture molecules has already been performed and which is thereafter fixed upon the disc for its specific reading.

Advantageously, each strip can be loaded with several different capture molecules that will react specifically with the same sample or different samples to be analyzed. Thereafter, the signal can be read individually or simultaneously upon the same disc. A classical disc like a compact-disc could be able to handle 20 or more of such strips.

Preferred embodiments that are most advantageous for manufacturing and operation of the compact-disc of the invention have dimensions within one or more of four pre-existing formats :

- 5 cm compact disk (CD), having a radius of about 3.8 cm and thickness of about 1 mm,
- 25 - 12 cm CD, having a radius of about 6 cm and a thickness of 1 mm,
- 20 cm CDV (commercially termed a "Laservision" disk), having a radius of 10 cm and a thickness of 2 mm, and
- 30 cm CDV disk, having a radius of 15 cm and a thickness of 2 mm.

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2. Fixation of capture probes on aminated CDs

2 solutions were prepared, one containing CMV capture probe and the other containing HIV capture probe. These solutions were MeIM 0.01 M pH 7.5 buffer containing
 5 denatured DNA capture probe (CMV or HIV) at a concentration of 2 $\mu\text{g/ml}$ and carbodiimide at a concentration of 1.6 mg/ml.

3 x 20 μl of these solutions were spotted on two aminated CDs and these CDs were incubated at 50 $^{\circ}\text{C}$ for
 10 5 hours in a wet atmosphere. After three washes of 5 min with NaOH 0.4 N + Tween 0.25% at 50 $^{\circ}\text{C}$, these CDs were rinsed 3 times with water and dried at 37 $^{\circ}\text{C}$ for 30 min.

3. Hybridization of CMV biotinylated DNA on CDs

15 Both CDs were incubated 5 min in NaOH 0.2 N for denaturing capture probe, then rinsed with 0.1 M maleate buffer pH 7.5 with 0.15 M NaCl. These CDs were then incubated in a hybridization solution containing
 20 denatured DNA salmon sperm 100 $\mu\text{g/ml}$, SSC 4X, Denhardt 5X and denatured CMV biotinylated DNA at a concentration of 70 ng/ml for 2 hours at 65 $^{\circ}\text{C}$. After hybridization step, the CDs were washed 3 times with 0.01 M maleate buffer containing 15 mM NaCl and TweenTM 0.3% at room temperature.

25 The first CD was then incubated with 0.1 M maleate buffer containing 0.15 M NaCl, 0.1% milk powder and streptavidin-peroxidase 1 $\mu\text{g/ml}$ for 45 min at room temperature. After conjugates incubation, both CDs were washed 3 times with 0.01 M maleate buffer containing 15 mM NaCl and Tween 0.3% at room temperature.

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4. Detection of hybridized DNA

The first CD was then incubated for 10 min in TMB solution (Medgenix). A picture was taken of this CD after 1 min of this incubation to see blue color appearing where positive hybridization occurred. The result can be obtained by absorption of transmitted light through the CD.

Example 2: Detection of DNA on CD with maser detection

The DNA capture probe was spotted on the CD surface and the hybridization with the target DNA were identical to the example 1. For the detection of the biotinylated hybridized DNA, the CD was incubated with 0.1 M maleate buffer containing 0.15 M NaCl, 0.1% milk powder and streptavidin-colloidal gold (Sigma, St-Louis, USA) 1 µg/ml for 45 min at room temperature. The CD was further incubated 30 min in a solution made of equal volume of Solution A and B from Silver enhancement kit (Sigma, St-Louis, USA) in order to have silver precipitate where positive hybridization occurred. This CD was recovered with a gold layer to allow a laser CD player to read information written on the CD and to read the interference due to silver precipitate (Fig. 2 and 3).

Example 3: Detection of protein on CD by light absorption

The CD used were partly inprinted with data on pits and this part was covered with gold. The fixation of the capture molecules was done on the periphery of the CD, directly on the plastic surface.

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1. Carboxylation of CD

First CDs were incubated 30 min in NaOH 1 N at room temperature then rinsed 3 times with water and dried at 37 °C for 30 min.

5

2. Fixation of antibodies on CDs

Three different types of antibodies were fixed on the carboxylated CD: antibodies against bovine serum albumin, antibodies against fluoresceine (for
10 negative control) and antibodies against streptavidin (for positive control).

20 µl of three different solutions of borate buffer 0.02 M NaCl pH 8.2 containing carbodiimide (Acros) at 1 mg/ml and one type of the three different antibodies
15 at 10 µg/ml were spotted on three different pieces of CD. These spots were incubated overnight at 4 °C, and then rinsed for 10 min with glycine buffer 0.1 M pH 9.2 containing casein at 0.1%, then twice with glycine buffer 0.1 M pH 9.2 containing Tween™ 20 at 0.1% for 5 min and
20 finally twice with glycine buffer 0.1 M pH 9.2. The CDs were dried at 37 °C during 30 min.

3. Detection of bovine serum albumin by ELISA technique on CD

25 The CDs were incubated at room temperature with the three different antibodies fixed onto the surface with a solution of serum albumin at 10 µg/ml in PBS containing 0.1% of casein. The incubation was for 90 min. The CDs were rinsed 3 times with PBS containing 0.1% of
30 Tween™ 20, and then incubated with biotinylated antibodies against serum albumin at 20 µg/ml in PBS containing 0.1% of

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casein for 45 min. They were then rinsed 3 times with PBS containing 0.1% of Tween™ 20, and then incubated for 45 min the CDs in a solution of PBS containing 0.1% of casein and either Streptavidin-peroxidase at 1 µg/ml. The CDs
 5 were rinsed 3 times with PBS containing 0.1% of Tween™ 20. For detection, the CD where streptavidin-peroxidase was fixed were incubated in a solution of TMB and pictures were taken after 2, 4 and 6 min under camera to see blue color appearing where we had spotted antibodies against BSA and
 10 against streptavidin.

Example 4: Detection of proteins on CD with laser detection

The albumin was spotted on the CD surface and the reaction with the antibodies were identical to the
 15 example 3. The conjugate used to react against the biotinylated antibodies was a streptavidin-gold. It. was incubated for 45 min in a PBS solution containing 0.1% casein at a concentration of 1 µg/ml. The streptavidin-gold served as a center for silver reduction. A solution of
 20 "silver enhancement" (Sigma) for 15 min at room temperature was used. Silver precipitation was seen at the place where antibodies against BSA and against streptavidin were spotted. A variation in the light absorption was observed, due to the precipitate and the size of the precipitate
 25 which are about 1 µm in diameter. The presence of pits was found by reflection of the laser beam (Fig. 5).

Example 5: Magnetic detection of DNA or protein on CD

Detection of hybridized DNA or protein on CD
 30 support can be achieved by magnetic process. Biotin bound to DNA or antibodies can be recognized by streptavidin conjugated to ferro-fluid (Immunicon, Huntington Valley,

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PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
 United States Patent and Trademark
 Office
 Box PCT
 Washington, D.C.20231
 ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 13 August 1999 (13.08.99)	
International application No. PCT/BE98/00206	Applicant's or agent's file reference P.FNDP.03/WO
International filing date (day/month/year) 24 December 1998 (24.12.98)	Priority date (day/month/year) 30 December 1997 (30.12.97)
Applicant REMACLE, José	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
 16 July 1999 (16.07.99)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Lazar Joseph Panakal

Telephone No.: (41-22) 338.83.38

TRAITE DE COOPERATION EN MATIERE DE BREVETS

PCT

RAPPORT DE RECHERCHE INTERNATIONALE

(article 18 et règles 43 et 44 du PCT)

Référence du dossier du déposant ou du mandataire P.FNDP.03/WO	POUR SUITE A DONNER voir la notification de transmission du rapport de recherche internationale (formulaire PCT/ISA/220) et, le cas échéant, le point 5 ci-après	
Demande internationale n° PCT/BE 98/ 00206	Date du dépôt international (jour/mois/année) 24/12/1998	(Date de priorité (la plus ancienne) (jour/mois/année) 30/12/1997
Déposant REMACLE JOSE		

Le présent rapport de recherche internationale, établi par l'administration chargée de la recherche internationale, est transmis au déposant conformément à l'article 18. Une copie en est transmise au Bureau international.

Ce rapport de recherche internationale comprend 3 feuilles.

☒ Il est aussi accompagné d'une copie de chaque document relatif à l'état de la technique qui y est cité.

1. Base du rapport

a. En ce qui concerne la **langue**, la recherche internationale a été effectuée sur la base de la demande internationale dans la langue dans laquelle elle a été déposée, sauf indication contraire donnée sous le même point.

☐ la recherche internationale a été effectuée sur la base d'une traduction de la demande internationale remise à l'administration.

b. En ce qui concerne **les séquences de nucléotides ou d'acides aminés** divulguées dans la demande internationale (le cas échéant), la recherche internationale a été effectuée sur la base du listage des séquences :

☐ contenu dans la demande internationale, sous forme écrite.

☐ déposée avec la demande internationale, sous forme déchiffrable par ordinateur.

☐ remis ultérieurement à l'administration, sous forme écrite.

☐ remis ultérieurement à l'administration, sous forme déchiffrable par ordinateur.

☐ La déclaration, selon laquelle le listage des séquences présenté par écrit et fourni ultérieurement ne vas pas au-delà de la divulgation faite dans la demande telle que déposée, a été fournie.

☐ La déclaration, selon laquelle les informations enregistrées sous forme déchiffrable par ordinateur sont identiques à celles du listage des séquences présenté par écrit, a été fournie.

2. ☐ Il a été estimé que certaines revendications ne pouvaient pas faire l'objet d'une recherche (voir le cadre I).

3. ☐ Il y a absence d'unité de l'invention (voir le cadre II).

4. En ce qui concerne le titre,

☐ le texte est approuvé tel qu'il a été remis par le déposant.

☒ Le texte a été établi par l'administration et a la teneur suivante:

METHOD COMPRISING CAPTURE MOLECULE FIXED ON DISC SURFACE

5. En ce qui concerne l'abrégé,

☒ le texte est approuvé tel qu'il a été remis par le déposant

☐ le texte (reproduit dans le cadre III) a été établi par l'administration conformément à la règle 38.2b). Le déposant peut présenter des observations à l'administration dans un délai d'un mois à compter de la date d'expédition du présent rapport de recherche internationale.

6. La figure des dessins à publier avec l'abrégé est la Figure n°

☒ suggérée par le déposant.

☐ parce que le déposant n'a pas suggéré de figure.

☐ parce que cette figure caractérise mieux l'invention.

4

☐ Aucune des figures n'est à publier.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/BE 98/00206

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 G01N33/543 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	EP 0 887 645 A (SUISSE ELECTRONIQUE MICROTECH ;PRIONICS AG (CH); SCHERRER INST PAU) 30 December 1998 see claims; figure 4E see column 8, line 12 - line 18 see page 11, line 51 - page 12, line 7 ----	1-29
P,X	EP 0 886 141 A (SUISSE ELECTRONIQUE MICROTECH ;PRIONICS AG (CH)) 23 December 1998 see claims; figure 4E see column 7, line 46 - line 56 see column 15, line 34 - line 41 ----- -/--	1-29

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

° Special categories of cited documents:

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- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

20 May 1999

Date of mailing of the international search report

01/06/1999

Name and mailing address of the ISA

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Fax: (+31-70) 340-3016

Authorized officer

Routledge, B

INTERNATIONAL SEARCH REPORT

International Application No

PCT/BE 98/00206

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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P,X	WO 98 15356 A (GORDON JOHN FRANCIS ;MOLECULAR DRIVES LIMITED (GB)) 16 April 1998 see claims see page 3, line 15 - line 16 see page 6, line 11 - line 24 see page 7, line 33 - page 8, line 15 see page 12, line 21 - page 13, line 19; figure 3 see page 18, line 16 - line 22 ---	1-29
P,X	WO 98 12559 A (DEMERS JAMES P) 26 March 1998 see claims 2,5 see page 7, paragraph 2 see page 8, paragraph 3 - page 9, paragraph 1 see page 15, paragraph 2 - page 18, paragraph 2 ---	1-29
X	WO 97 21090 A (GAMERA BIOSCIENCE) 12 June 1997 cited in the application see claims 1,14-21,30-63 see page 6, line 2 - line 7 see page 11, line 2 - line 28 see page 28, line 11 - page 29, line 14 see page 52, line 3 - page 53, line 30 ---	1-29
X	WO 96 09548 A (GORDON JOHN FRANCIS ;UNIV DUNDEE (GB)) 28 March 1996 see claims see page 4, line 14 - page 5, line 8 see page 6, line 3 - line 17 see page 11, line 5 - line 20 see page 14, line 5 - line 18 -----	1-29

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/BE 98/00206

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0887645 A	30-12-1998	EP 0886141 A	23-12-1998
EP 0886141 A	23-12-1998	EP 0887645 A	30-12-1998
WO 9815356 A	16-04-1998	AU 4564297 A	05-05-1998
WO 9812559 A	26-03-1998	AU 4428497 A	14-04-1998
WO 9721090 A	12-06-1997	AU 702403 B	18-02-1999
		AU 1283397 A	27-06-1997
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TRAITE DE COOPERATION EN MATIERE DE BREVETS

PCT

RAPPORT DE RECHERCHE INTERNATIONALE

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INTERNATIONAL SEARCH REPORT

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Name and mailing address of the ISA

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Routledge, B

INTERNATIONAL SEARCH REPORT

International Application No

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WO 9721090	A	12-06-1997	AU 702403 B	18-02-1999
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